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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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PATENT DEPARTMENT
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EXAMINER
CHEU, CHANGHWA J

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,629	KNOX ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on 10/19/01

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. (For example, the spelling of "polarisation" should be –polarization.)

In claim 1, line 3, it is unclear how the assay is performed (for example, it is unclear whether a sample is required in the assay, what steps are required in the assay...)

In claim 1, lines 8-9, it is unclear as to what steps are required to generate further assay results.

The term "compared to known assay techniques" in claim 15, line 3, is a relative term which renders the claim indefinite. The term "known assay techniques" is not defined by the claim, the specification does not provide a standard for ascertaining the

requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

In claim 28, line 3, the phrase "other suitable container" renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "other suitable container", thereby rendering the scope of the claims unascertainable. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

I. Claims 1-7, 9, 12, 16-18, 21, 23, 27 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Pines et al., 6,426,058. Pines et al. disclose using an assay reagent (see column 12, lines 6-27) containing at least one NMR active nucleus (see column 15, lines 37-41) to perform an assay, and hyperpolarizing at least one NMR active nucleus (see column 18, lines 43-45) and analyzing the assay reagent and/or the assay by NMR and optionally using the NMR data obtained to generate further assay results (see column 18, lines 61-64).

As to claims 2 and 3, the NMR active nucleus is ^{13}C or ^{15}N, see column 15, lines 39.

As to claims 4 and 5, the assay reagent is a compound which contains an artificially high concentration of an NMR active nucleus, in 1-10 defined positions, see column 12, lines 6-26.

As to claim 6, the assay reagent is an organic compound comprising one or more NMR active nuclei associated with a bond which is broken during the course of the assay, see column 12, lines 6-26.

As to claim 7, each NMR active nucleus produces a distinct NMR spectrum as claimed, see column 4, lines 13-24.

As to claim 9, the assay reagent is a nucleotide, or nucleotide analogue, polynucleotide, amino acid analogue, polypeptide or protein, see column 12, lines 6-15.

As to claim 12, the assay reagent is a compound labeled with at least one NMR active nucleus and an excretion product of the assay reagent are hyperpolarized and analyzed by nuclear magnetic resonance spectroscopy, nuclear magnetic resonance imaging or both, see column 8, lines 9-17.

As to claim 16, the hyperpolarization is carried out by polarization transfer from a hyperpolarized noble gas, see column 9, lines 6-10.

As to claim 17, the noble gas is ^{129}XE, see column 9, line 10.

As to claim 18, the noble gas is ^{3}He, see column 9, line 7.

As to claim 21, the polarization transfer uses dynamic nuclear polarization, see column 2, lines 34-37.

As to claim 23, the hyperpolarization is carried out with the spin refrigeration technique, see column 8, lines 25-30.

As to claim 27, the analyzing step is performed in an aerosol or flow-through device applied to aerosol droplets where the well, surface or container is used to contain the assay reagent, see column 8, lines 21-25.

As to claim 28, a kit is disclosed, which comprises an assay reagent containing at least one NMR active nucleus contained in a well or vial or container, see column 8, lines 21-25.

II. Claims 1-7, 9, 12, 16-18, 21-23, 27 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Ardenkjaer-Larson et al., 6,278,893.

As to claims 1 and 22, Ardenkjaer-Larson et al. disclose using an assay reagent containing an NMR active nucleus, hyperpolarizing the nucleus, see column 24, lines 43-45, and analyzing the assay by NMR, wherein the hyperpolarization is carried out by para hydrogen induced polarization, see column 18, lines 6-7.

As to claims 2 and 3, the NMR active nucleus is ^{13}C, see column 2, line 46.

As to claims 4 and 5, the assay reagent is a compound which contains an artificially high concentration of an NMR active nucleus, in 1-10 defined positions, see column 2, line 46.

As to claim 6, the assay reagent is an organic compound comprising one or more NMR active nuclei associated with a bond which is broken during the course of the assay, see column 18, lines 21-45.

As to claim 7, each NMR active nucleus produces a distinct NMR spectrum as claimed, see column 2, lines 30-40.

As to claim 9, the assay reagent is a nucleotide, or nucleotide analogue, polynucleotide, amino acid analogue, polypeptide or protein, see column 2, lines 5-10.

As to claim 12, the assay reagent is a compound labeled with at least one NMR active nucleus and an excretion product of the assay reagent are hyperpolarized and analyzed by nuclear magnetic resonance spectroscopy, nuclear magnetic resonance imaging or both, see column 24, lines 43-45, and column 18, lines 6-7.

As to claim 16, the hyperpolarization is carried out by polarization transfer from a hyperpolarized noble gas, see column 22, line 60.

As to claim 17, the noble gas is ^{129}XE, see column 22, line 60.

As to claim 18, the noble gas is ^{3}He, see column 22, line 61.

As to claim 21, the polarization transfer uses dynamic nuclear polarization, see column 13, line 15.

As to claim 23, the hyperpolarization is carried out with the spin refrigeration technique, see column 23, lines 20-33.

As to claim 27, the analyzing step is performed in an aerosol or flow-through device applied to aerosol droplets where the well, surface or container is used to contain the assay reagent, see column 23, lines 29-33.

As to claim 28, a kit is disclosed, which comprises an assay reagent containing at least one NMR active nucleus contained in a well or vial or container, see column 23, lines 29-33.

III. Claims 1-29 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Golman et al., 6,574,496.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

IV. Claims 8, 14, 15, 19, 20, 24-26 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pines et al., 6,426,058. Pines et al. disclose the invention substantially as claimed (see above.)

However, Pines et al. does not disclose the following: the assay reagent is analyzed at known time intervals to generate information about a change with time of the assay reagent (see claim 8); the hyperpolarization transfer is repeated to enhance the signal-to-noise ratio (see claim 14); the shortening effect as expressed by the improvement of signal-to-noise per unit time is a factor of 10 or more compared to known assay techniques without hyperpolarization (see claim 15); the noble gas is in a solution and the viscosity of the solution is at least 1000 mPs (see claim 19); the hyperpolarization transfer is carried out at a temperature of 4.2 K or less in the presence of a magnetic field of at least 1T (see claim 20); more than one assay is multiplexed and monitored by NMR spectroscopy and/or NMR imaging (see claim 24); the assay is

performed in a multiwell or multispot assay array (see claim 25); the analyzing step is performed by using both NMR spectroscopy and magnetic resonance imaging, and repeating the examination at least once (see claim 26); the NMR analysis step is carried out in the same well or vial or container as the hyperpolarization transfer is carried out (see claim 29.)

Pines et al. does however disclose that the hyperpolarized noble gas may be in liquid, solid or gas phase, see column 8, lines 22, and that the noble gas can be combined with a fluid to form a mixture, see column 8, lines 53-54, and lines 64-67, and that it is desirable to freeze the gas in a magnetic field (see column 8, lines 27-29), and that the result can be analyzed using both NMR spectroscopy and magnetic resonance imaging (see column 8, lines 60-63.)

It would have been obvious to provide the noble gas in a solution having the viscosity as claimed, or to hyperpolarize at the temperature and magnetic field as claimed, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

Furthermore, it would have been obvious to analyze at time intervals, to repeat the analysis steps, to analyze more than one multi-assay array, and to perform the NMR analysis step in the same well or vial or container as the hyperpolarization transfer is carried out, since it is generally recognized that repeating known steps to obtain further data, or to analyze more than one sample at a time using known methods involves only routine skill in the art.

V. Claims 10, 11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pines et al., 6,426,058, in view of Yu, 6,103,492. Pines et al. disclose the invention substantially as claimed (see above.)

Howver, Pines et al. do not disclose that the assay is a nucleic acid hybridization assay (see claim 10), that the assay is a binding assay (se claim 11), nor that the assay is a binding study using micro-organisms or cultured cells (see claim 13.)

Yu however discloses an assay method (see column 8, lines 45-59), wherein the assay is a nucleic acid hybridization assay, see column 8, lines 60-67, the assay is a binding assay, see column 8, lines 45-59, or column 9, lines 8-19, and the assay is a binding study using micro-organisms or cultured cells, see column 36, lines 29-32. Yu discloses use of isotopically labeled reagents in conjunction with spectroscopy, such isotopes being ^{13}C or ^{15}N, see column 40, lines 39-44. Yu also discloses use of NMR spectroscopy for analysis of an interaction between an agent and a receptor, see column 40, lines 37-45, and column 41, lines 41-48.

Thus, since Yu teaches use of NMR spectroscopy with the same NMR active nucleus, i.e., ^{13}C or ^{15}N, as Pines, and Pines teaches use of hyperpolarized noble gases to enhance and improve NMR and MRI, it would have been obvious to combine the references and thus hyperpolarize the compounds having ^{13}C or ^{15}N active nucleus in the Yu method in order to enhance and improve the NMR and MRI steps.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Keating et al., 6,207,383, discloses use of NMR spectroscopy and hyperpolarization techniques.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is (703) 306-5560. The examiner can normally be reached on M-TH 8-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703)305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

A.L.
June 30, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

06/30/03